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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/134,333	08/14/1998	SHIRLEY LONGACRE-ANDRE	0660-0135-0X	7863

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EXAMINER	
GRUN, JAMES LESLIE	

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
12/15/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/134,333	LONGACRE-ANDRE ET AL.	
	Examiner	Art Unit	
	JAMES L. GRUN	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *134,139-142,145,148-155,157,158,160,161,163,164 and 166-177* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *134,139-142,145,148-155,157,158,160,161,163,164 and 166-177* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

The amendment filed 02 September 2008 is acknowledged and has been entered. Claims 134, 139-142, 145, 148-155, 157, 158, 160, 161, 163, 164, and 166-177 remain in the case.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 145, 149, and 150 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 145, 149, and 150, it is not clear what is encompassed by "an aimmune response."

Applicant's arguments filed 02 September 2008 have been fully considered but they are not deemed to be persuasive. Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

Claims 134, 145, 176, 177, and claims dependent thereupon are objected to because of the following informalities: it is believed that --parasitemia-- was intended. Appropriate correction is required.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
(c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 153, 169, 172, and 175 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Longacre (Mol. Biochem. Parasitol. 74: 105-111, 1995) in view of Longacre et al. (Mol. Biochem. Parasitol. 64:191, 1994) for reasons of record.

Claims 134, 139-141, 145, 148-150, 176, and 177 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Longacre in view of Longacre et al., and further in view of Holder et al. (US 5,720,959) for reasons of record in the prior rejection of the similar subject matter of these claims.

Claims 151, 152, 154, 155, 157, 158, 160, 161, 163, 164, 166, 167, 168, 170, 171, 173, and 174 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Chappel et al (Mol. Biochem. Parasitol. 60:303, 1993), Miller et al (Mol. Biochem. Parasitol. 59:1, 1993), Longacre et al (Mol. Biochem. Parasitol. 64:191, 1994), and Longacre (Mol. Biochem. Parasitol. 74: 105-111, 1995) for reasons of record in the prior rejection of the similar subject matter of these claims.

Claims 134, 139-142, 148, 150, 176, and 177 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chappel et al., Miller et al., Longacre, and Longacre et al., and further in

view of Holder et al. (U.S. Pat. No. 5,720,959) for reasons of record in the prior rejection of the similar subject matter of these claims.

Applicant's arguments filed 02 September 2008 have been fully considered but they are not deemed to be persuasive.

Applicant urges that the references do not specifically teach an effective vaccine, particularly one comprising alum. This is not found persuasive for a number of reasons. Firstly, the argument is unpersuasive because a recitation of intended use is accorded patentable weight only to the extent that it limits the actual components of a composition; in the instant case the intended use does not affect the recombinant protein as claimed in any way which distinguishes over the subject matter taught or suggested by the references as set forth in the rejections of record. Secondly, the argument is also not found persuasive because the missing teaching is clearly provided by the combination of the references with the teachings of Holder et al. which provide the direct suggestion to use alum as adjuvant for an MSP-1 fragment vaccine. Thirdly, the argument is also not found persuasive because the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. Notwithstanding applicant's assertions to the contrary, as notoriously old and well known in the art as taught in the references and as set forth in the rejections of record, one would have expected fragments of various lengths comprising the conformational epitopes of the EGF-like domains of the p19 fragments of plasmodial MSP-1 proteins to function in a vaccine. As set forth, notwithstanding

applicant's assertions to the contrary, variable levels of parasitemias in non-inbred hosts were also not found persuasive or an unexpected result.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

For example, in this regard, applicant urges that Longacre (1995) merely describes the gene sequence of the *P. cynomolgi* MSP-1 p42 for sequence comparisons and makes no mention of cloning a C-terminal fragment. This is not found persuasive because the reference teaches the cloning of the *P. cynomolgi* MSP-1 C-terminal fragments as a step to vaccine trials with the fragments of the protein (see e.g. pages 105-107, especially the ¶ bridging pages 106-107) and specifically teaches the use of a recombinant baculovirus for expression of the *P. cynomolgi* MSP-1 protein fragment comprising the p19 fragment (see e.g. ¶ bridging pages 108-109).

Applicant urges that Longacre (1995) fails to teach the use of a fragment having the sequence from amino acid residues 276-380 as the 19kDa C-terminal fragment, that one would not have expected the C-terminal fragments, especially the 19kDa C-terminal fragment, to function in a vaccine, and that there is no motivation to combine the teachings of Longacre in view of Longacre et al., and further in view of Holder et al. Notwithstanding applicant's implications to the contrary, the instant use of "comprising" claim language, e.g. in claim 134, does not exclude a longer recombinant protein, as cloned in Longacre, that contains the relevant fragment as instantly claimed. Applicant has provided no description or evidence that inclusion

of other residues of the longer sequence materially changes the character of the composition as both the shorter and longer sequences include the EGF-like domains notoriously well known to the art. Indeed, the recombinant protein expressed in Longacre (1995), with a construct containing the N-terminal signal sequence of *P. vivax*, containing residues Met_1-Asp_{32} therein, with *P. cynomolgi* MSP-1 in view of Longacre et al. (see above and Fig. 1 legend in Longacre (1995) disclosing the use of the $pVLSV_{200}$ plasmid of Longacre et al.), contained relevant conformational epitopes of the p19 fragment (again see page 109). This is also not found persuasive because one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In this regard, the examiner also recognizes that references cannot be arbitrarily combined and that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See: *In re Nomiya*, 184 USPQ 607 (CCPA 1975); *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); or, *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). However, there is no requirement that the claimed invention or a motivation to make the modification be expressly articulated in any one or all of the references. The test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. See: *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re McLaughlin*, 170 USPQ 209 (CCPA 1971). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. *In re Bozek*, 163 USPQ 545 (CCPA 1969). A person of ordinary skill in the art, using common knowledge and common sense, is capable of

fitting the teachings of multiple references together like pieces of a puzzle, regardless of the specific problem being addressed by the individual references. Any need or problem known at the time of the invention can provide a reason for combining elements of the different references. A person of ordinary skill in the art is also a person of ordinary creativity. In this case, for the reasons of record, ample motivations have been set forth to clone and produce the C-terminal p42 and p19 fragments of MSP-1 proteins as notoriously old and well known vaccine candidates in the art as clearly taught by the references (see e.g.: Longacre at al., page 192; Longacre, pages 105-107). Moreover, the examiner would further note the identification of the p42 and p19 cleavage sites in Fig. 1 of Longacre and the teaching in Longacre et al. to include 6 or 7 of the apparently well conserved residues upstream from the cleavage sites in p42 and p19 constructs (see e.g. page 194, col. 2). Such teachings would guide one to residues 276-380 of instant SEQ ID NO: 11, and to the sequence in Longacre, for a *P. cynomolgi* MSP-1 p19 construct. As set forth, Holder et al. teach the incorporation of MSP-1 peptides comprising the EGF domains in vaccine compositions comprising alum.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

For example, in this regard, applicant urges that Holder et al. do not teach proteins of malarial parasites infectious for man made recombinantly with a baculovirus. This is not found persuasive in view of the combined teachings of Longacre and Longacre et al. or the combined

teachings of Chappel et al., Miller et al., Longacre, and Longacre et al. Moreover applicant's assertion that Holder et al. teach the sequences of a MSP-1 protein from a murine parasite were not found persuasive because the cited reference (US 5,720,959) teaches *P. falciparum* MSP-1 protein fragments as well as murine fragments.

Moreover, the exercise of pairing the teachings of only some of the cited references, as argued by applicant, is equally unpersuasive. For example, in this regard, applicant urges that the combination of Chappel et al. and Miller et al. only teach cloning of a the *P. falciparum* MSP-1 p42 construct. This is not found persuasive in view of the combined teachings of the references of record.

In response to Applicant's arguments that there are no specific suggestions to combine the references of Chappel et al., Miller et al., Longacre, and Longacre et al., and further in view of Holder et al., the examiner recognizes that references cannot be arbitrarily combined and that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the common knowledge or common sense generally available to one of ordinary skill in the art. See: *In re Nomiya*, 184 USPQ 607 (CCPA 1975); *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); or, *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). However, there is no requirement that the claimed invention or a motivation to make the modification be expressly articulated in any one or all of the references. The test for combining references is what the combination of disclosures, taken as a whole, would suggest to one of ordinary skill in the art. See: *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); or, *In re McLaughlin*, 170 USPQ 209 (CCPA 1971). References

are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. See: *In re Bozek*, 163 USPQ 545 (CCPA 1969). A person of ordinary skill in the art, using common knowledge and common sense, is capable of fitting the teachings of multiple references together like pieces of a puzzle, regardless of the specific problem being addressed by the individual references. Any need or problem known at the time of the invention can provide a reason for combining elements of the different references. A person of ordinary skill in the art is also a person of ordinary creativity. In this case, for the reasons of record, ample motivations have been set forth to clone and produce the C-terminal p42 and p19 fragments of MSP-1 proteins comprising the conformational epitopes of the EGF-like domains as notoriously old and well known vaccine candidates in the art as clearly taught by the references (see e.g.: Chappel et al.; Longacre at al., page 192; Holder et al.; Longacre, pages 105-107). As set forth, one would have had a reasonable expectation of the successful use of a plasmid containing the N-terminal signal sequence of *Plasmodium vivax*, containing residues Met_1-Asp_{32} therein, to function in the cloning of a heterologous species MSP-1 fragment in view of its already successful use therefor as taught in Longacre in view of Longacre et al. As set forth, Holder et al. teach the incorporation of MSP-1 peptides comprising the EGF domains in vaccine compositions comprising alum. Moreover, the examiner would further note the identification of at least the p19 cleavage site in Miller et al. (see e.g. pages 6 and 10) and the teaching in Longacre et al. to include 6 or 7 of the apparently well conserved residues upstream from the cleavage sites in p42 and p19 constructs (see e.g. page 194, col. 2). Such teachings would guide one to appropriate residues for the *P. falciparum* MSP-1 p19 construct. Further, notwithstanding applicant's assertions to the contrary, the instant use of open claim language does not exclude a longer

recombinant protein, as cloned in Chappel et al., that comprises the relevant fragment as instantly claimed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR REPLY TO THIS FINAL ACTION IS SET TO EXPIRE **THREE MONTHS** FROM THE MAILING DATE OF THIS ACTION. IN THE EVENT A FIRST REPLY IS FILED WITHIN **TWO MONTHS** OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE **THREE-MONTH** SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR REPLY EXPIRE LATER THAN **SIX MONTHS** FROM THE MAILING DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 11 a.m. to 7 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, SPE, can be contacted at (571) 272-0806.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/J. L. G./
James L. Grun
Examiner, Art Unit 1641
December 13, 2008

/Ann Y. Lam/
Primary Examiner, Art Unit 1641
December 7, 2008